UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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MEDICAL DEVICES ADVISORY COMMITTEE

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GASTROENTEROLOGY AND UROLOGY DEVICES
ADVISORY PANEL MEETING

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Friday,
August 17, 2001

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The Committee was called to order at 9:41 a.m., at the Food and Drug Administration, 9200 Corporate Boulevard, Conference Room 20B, Rockville, Maryland 20850 by Chairman Anthony N. Kalloo, M.D., presiding.

PANEL MEMBERS PRESENT:

DR. ANTHONY N. KALLOO, Chairperson
DR. JEFFREY COOPER, Executive Secretary
DR. MARY GELLENS, Member
DR. ARTHUR D. SMITH, Member
DR. JOSEPH H. STEINBACH, Member
DR. KAREN WOODS, Member
MS. KAREN NEWMAN, Member
MR. MICHAEL S. BANIK, Member
DR. MICHAEL EPSTEIN, Member
DR. WALTER KOLTUN, Member
DR. STEVEN MCCLANE, Member
DR. MARK A. TALAMINI, Member
DR. NANCY BROGDON, FDA Representative

PUBLIC SPEAKERS:

NANCY LOITZ
LARRY GETLIN
DAVID WORRELL
DR. DOUGLAS WONG
DR. SUSAN CONGILOSI
DR. ARON YUSTEIN
KATHLEEN OLVEY

C-O-N-T-E-N-T-S

P-R-O-C-E-E-D-I-N-G-S

(9:41 a.m.)

CHAIRMAN KALLOO: Good morning. Welcome to the Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee. My name is Anthony N. Kalloo, and before we proceed any further, I would like to hand the meeting over to Jeffrey Cooper, the Executive Secretary for the Committee.

SECRETARY COOPER: Good morning. I would like to read a statement concerning the appointments to temporary voting status. Pursuant to the authority granted under Medical Devices Advisory Committee Charter, dated October 27th, 19990, and as amended August 18th, 1999, I appoint Michael Epstein, M.D., Walter A. Koltun, M.D., Steven McClane, M.D., Mark A. Talamini, M.D., and Lawrence Way, M.D., as voting members for the Gastroenterology and Urology Devices Advisory Panel for this meeting on August 17th, 2001.

For the record, that there are special government employees and consultants to this panel or other panels under the Medical Devices Advisory Committee. They have undergone the customary conflict

of interests review and reviewed the materials to be considered at this meeting, signed by the Director, Center for Devices and Radiological Health.

The following announcement addresses conflict of interests associated with this meeting, and is made a part of this record to preclude even the appearance of an impropriety, and to determine if any conflicts exist, and that the Agency review the submitted agenda, and all financial interests reported by the Committee participants.

The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employer's financial interests.

However, the Agency has determined that participation of certain members and consultants, the need for whose services outweighs the potential conflict of interest involved, is in the best interest of the government.

We would like to note for the record that the agency took into consideration a certain matter regarding Dr. Arthur Smith. He reported an interest

in a firm at issue, but in matters that are not related to today's agenda. Therefore, the Agency has determined that he may participate fully in today's deliberations.

In the event that the discussions involve any other products or firms not already on the agenda for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement, and the exclusion will be noted for the record.

With respect to all the other participants, we ask in the interest of fairness that all persons making statements or presentations disclose any current or previous financial involvement with any firm whose products they may wish to comment upon.

On another note, we have the tentative 2002 panel meeting dates, and they are February 1st, 2002, and May 17th, 2002, August 9th, 2002, and November 7th, 2002. Thank you.

CHAIRMAN KALLOO: We will now proceed ot the open public hearing session of this meeting. If

there is anyone wishing to address the panel, please raise your hand, and you may have an opportunity to speak.

I would ask at this time that all persons addressing the panel come forward to the microphone and speak clearly as the transcriptionist is dependent on this means of providing an accurate transcription of the proceedings of the meeting.

Before making your presentation to the panel, state your name and affiliation, and the nature of any financial interests you may have with the topic that you are going to present.

Each presenter can be allotted 10 minutes. Please provide a copy of your remarks and any visual aids to the transcriptionist. Dr. Cooper has received one written set of comments.

SECRETARY COOPER: And that is the National Association for Continence has submitted a request for approval of the device, and copies of that letter are available at the desk.

CHAIRMAN KALLOO: We have one scheduled presenter, and we will begin with Nancy Loitz.

MS. LOITZ: Good morning. My name is Nancy Loitz, and I am a recipient of the artificial bowel sphincter, and I am here to try and put a human face on the matter under consideration today. Excuse me for the emotion.

But it is has been a long journey, and one that I am very proud to speak about today. I am going to read my written remarks, but I would be very open to any questions that the panel might have.

In November of 1997, as I sat down for Thanksgiving Dinner with friends, we began our annual ritual of sharing with the group the one thing for which we were most thankful.

And that year my choice was easy. I am thankful, I said, for my new sphincter. We all laughed, but everyone at that table understood the significance of my statement, since as my closest friends, they had witnessed my struggle prior to receiving my implant, and they had seen me joyfully reclaim my life afterward.

Today, I thank you for allowing me to be here. Preparing to tell my story today has given me

the opportunity to reflect upon it myself. It had been a while I had thought much about what life was like before receiving my implant.

I had just gotten too busy getting on life. I am afraid that I had begun to take it for granted. The medical journey that has led to my appearance today began in 1993, when I underwent a bowel resection to repair a complete rectal prolapse, a condition that I had had since childhood.

The surgery, performed by a general surgeon in my hometown of Bloomington, Illinois, was only partially successful, and within two years the prolapse returned. Wit it became the beginning of a gradual, and ultimately a complete, loss of bowel control.

At this time, I was a 36 year old single woman. I had always lead a very active life. I had a rewarding and successful career as a professor of theater, and I enjoyed hiking, working out at the gym, and an occasional bike ride.

And being a rather stubborn person, I initially refused to allow my incontinence to affect

the way I lived my life. I was lucky that the onset of my condition was gradual.

Over time, I developed an intricate system of coping mechanisms. I had spare undergarments stashed everywhere -- in my purse, in the desk drawer at work, in the glove compartment of my car.

I prided myself on knowing where every public bathroom in Bloomington, Illinois, was located. And, of course, I always carried with me a complete change of clothes for those times when I didn't get to one in time.

Despite my absolute determination not to let this condition rule my life, it eventually worsened to the point that those around me couldn't help but notice that something was wrong.

My incontinence became so severe that I had to leave class, rehearsals, or meetings, sometimes as several times in an hour, to address the almost constant leaking.

I began to exercise at home since physical activity exacerbated my problem, and working out at the gym guaranteed a major accident in a public

location, something I got very good at negotiating around.

The use of enemas, for example, prior to special events such as weddings, opening night performances, or air travel, allowed me to continue to participate fully in such activities without having to share with anyone the severity of my condition.

While normally I was pretty successful at not letting my physical problem get the best of me, a day came in April of 1966 when I had frankly had enough. It had been what I jokingly referred to as a "BBD" or a particularly "Bad Bowel Day."

And that night I made a phone call to an old friend, and it was a phone call that would change my life. An engineer at American Medical System, Bob is the husband of a woman with whom I had worked for a short time nearly 15 years before.

For some reason, on that night I remembered the conversations that we had had many years before about the products that they made at AMS. On this evening 14 years later, it dawned on me that the solution to my problem would be an artificial

bowel sphincter, and if anybody made such a thing, it would be AMS.

Since Bob knew nothing of my medical condition, I caught him a bit off-guard when I called him out of the blue, and I asked does AMS make an artificial bowel sphincter.

Unsure whether he could share information about the study, Bob put me in touch with Cari Voda from AMS, who suggested that I contact Dr. Douglas Wong. Within a week, I sat in Dr. Wong's office, hoping desperately to be a part of the clinical trial of the AMS artificial bowel sphincter.

Although Dr. Wong agreed that I might eventually benefit from the implant, he dod not rush to include me in the study. He suggested that first he surgically repair my recurrent prolapse, a procedure that had the possibility of alleviating the incontinence as well.

Unfortunately, it did not. We then tried biofeedback in a hope that I could retrain my sphincter muscle to do the job that it was intended to do. Still, there was no improvement in my condition.

Having exhausted all other possibilities, it was only now that Dr. Wong determined that I was a suitable candidate for the implant, and agreed to include me in the clinical trial.

My first implantation surgery took place in June of 1997. Despite a 9-day hospital stay due to unexplained high fevers, the surgery was a complete success. The improvement in my condition was immediate and profound.

I need not go into detail about life after receiving the implant, since life with the implant is simply that, life. I now had complete control of my bowels for the first time in years. Suddenly I felt like I had my life back.

And with it came possibilities that I had abandoned during the peak of my medical difficulties. Although I had always hoped to have children, my health problems had made single parenthood out of the question.

But on March 10th, 1999, less than two years after receiving my first implant, I gave birth by caesarean section to my daughter, Zoe. My implant

continued to function perfectly throughout my pregnancy, and for more than a year following my daughter's birth.

Last summer, however, I detected that something had changed with the device. Tests confirmed that fluid had leaked from my implant and a revision surgery would be necessary. I felt no need to rush forward with the second surgery since life with the implant, even when it was broken, was far superior to life without one.

I did, however, begin experience enough occasional episodes of incontinence that I decided that it made sense to go forward with the replacement. My revision surgery was performed 12 weeks ago today by Dr. Susan Congilosi.

It was determined at that time that the leak in my first device was due to a stress tear in the cuff. Although the surgery went well, I later developed an infection near the site of the abdominal incision.

I am delighted to report that following a long course of antibiotics, I am now free of infection

and am again in possession of a fully functioning AMS Artificial Bowel Sphincter.

My journey to this place has not been without difficulty. But now once have I regretted by decision to get on board. At each bump in the road -- during the fevers following my first surgery, when we discovered the leak in my first device, when I developed the infection following my revision -- what I always feared most was that I could lose the implant.

I knew all too well what life was like without it, and now that I have it, I am not giving it back. I would like to close today with one last offer of thanksgiving to those people who have been with me at teach stage of this adventure.

Thank you to Dr. Wong, to Dr. Congilosi, to Linda Jensen, and to the staff at AMS. Thank you for making an investment in me. You have given me a really great gift.

And I hope that by being here today I can contribute in at least a small way to making that same gift available to others who are suffering now as I

once did. Thank you.

CHAIRMAN KALLOO: Thank you, Ms. Loitz. For the sake of completeness could you tell us if you have any financial interests in the company AMS?

MS. LOITZ: I do not.

CHAIRMAN KALLOO: Thank you.

DR. STEINBACH: Do you know if your first sphincter was an early model or the new improved one?

MS. LOITZ: I don't know.

DR. STEINBACH: Maybe you are the wrong person to ask.

MS. LOITZ: Oh, it was the new one.

CHAIRMAN KALLOO: Okay. Thank you, Ms. Loitz. Are there any other public comments? If not, Jeff.

DR. COOPER: I wanted to go about and do the introductions. The first thing I wanted to do was introduce Nancy Brogdon. She was recently named the Director of the Division of Reproductive Abdominal and Radiological Devices. She is microbiologist with several years of clinical laboratory experience.

She was most recently the Deputy Director

of the Division of Athalmec, and Ear, Nose, and Throat Devices.

In that division, she had been a scientific reviewer, and held various division management positions, including interim director for a total of 21 years, and we welcome her to our division.

DR. BROGDON: Thank you.

DR. COOPER: Would each member of the panel him or herself, designate your specialty, position, title, institution, and status on the panel, whether you are a voting member or consultant, or temporary voting member, industry rep, or consumer rep, and we will start with Dr. Talamini.

DR. TALAMINI: Mark Talamini, Associate Professor of Surgery, at the Johns Hopkins University School of Medicine, temporary voting member.

DR. MCCLANE: Steven McClane, and I am a colorectal surgeon, Stamford, Connecticut, and I am a temporary voting member.

DR. GELLENS: Mary Gellens, Associate Professor of Nephrology, St. Louis University, and I

am a standing voting member.

DR. EPSTEIN: I am Michael Epstein, Annapolis, a Gastroenterologist, temporary voting member.

DR. BROGDON: Nancy Brogdon.

MR. BANIK: Michael Banik, Vice President of R&D, Boston Scientific, Industry Representative and non-voting member.

DR. COOPER: We have two people who have not come yet, and I am not sure if they are or not, and that is Diane Newman, who is our Consumer Rep; and Dr. Lawrence Way.

DR. KOLTUN: Dr. Walter Koltun, and I am an associate professor of surgery at the Penn State University Hershey Medical Center.

DR. STEINBACH: Joseph Steinbach, associate project biomathematician, at the University of California at San Diego.

DR. WOODS: Karen Woods, and I am a clinical associate professor of medicine at Baylor College of Medicine, in Houston, and I am a gastroenterologist, and in private practice.

DR. SMITH: Arthur Smith, and I am a urologist, a Professor of Urology at Albert Einstein College of Medicine, and I am a voting member.

CHAIRMAN KALLOO: I am Tony Kalloo, and I am the Panel Chair, and an associate professor of medicine at Johns Hopkins University, and clinical director for the division of gastroenterology.

DR. COOPER: And I am Jeff Cooper, the Executive Secretary for the FDA.

CHAIRMAN KALLOO: Okay. We will now proceed to the open committee discussion. We will start with the sponsor's presentation of PMA PO10020, from American Medical Systems for the AMS Acticon Neosphincter, for the treatment of fecal incontinence.

I would ask at this time that all persons addressing the panel come forward to the microphone and speak clearly, as the transcriptionist is dependent on this means of providing an accurate transcription of the proceedings of the meeting.

Before making your presentation to the panel, state your name and affiliation, and the nature of your financial interests in that company. Let me

quickly remind you that a definition of financial interest in the sponsor company may include compensation for time and services of clinical investigators, their assistants and staff, in conducting the study, and in appearing at the panel meeting on the behalf of the applicant; a direct stake in the product under review, that is, inventor of the product, patent holder, owner of shares of stock, et cetera, an owner or part-owner of the company.

And of course no statement is necessary from employees of that company. I would like to remind the panel that it may ask for clarification of any points included in this sponsor's presentation.

The first speaker as listed on the agenda is Larry Getlin, a vice president of regulatory medical affairs and quality systems.

MR. GETLIN: Mr. Chairman, distinguished panel members, good morning. My name is Larry Getlin, and I am the vice president of regulatory and medical affairs for American Medical Systems.

And we are very pleased this morning to present our data in support of our pre-market

application for the Acticon Neosphincter to treat patients with severe fecal incontinence.

And before I present our agenda for this morning, what I would like to do is just provide you with a few brief comments. We believe that the clinical data, the results that you will see today, and that are also in your panel packs, will be clarified, and they indicate three things.

One, that we have met the primary and secondary end points for the study. And, number two, the device is safe and effective to treat patients with severe fecal incontinence; and, three, that the device is one that will be able to be used for the patients that are so indicated.

Also, this device presents, and the data, a compelling benefit to risk ratio for patients who basically have lost all other options to treat their fecal incontinence, and has virtually left them housebound, and has significantly impacted their quality of life.

In addition the Acticon Neosphincter device, although designed specifically to treat fecal

incontinence, severe fecal incontinence, is not a new device, and I say that because the Acticon Neosphincter device is essentially the same device as the AMS artificial urinary sphincter, which has been in the marketplace for over 28 years, and has an approved PMA to treat severe -- I'm sorry, urinary incontinence as a result of ISD following prostate surgery.

At this time, I would like to just cover a presentation. Mr. David Worrell, who is a project lead on this for the regulatory group, and senior regulatory specialist, will cover the indications for us, and the device indication and history.

Dr. Douglas Wong, principal investigator, will cover the effectiveness results. Dr. Susan Congilosi, who happens to also have implanted more artificial bowel sphincters in the U.S. than any other physician, will present the safety results.

And Mr. Worrell will then conclude with AMS' summary statements and remarks. I have one footnote for Dr. Wong. Dr. Wong will be departing at 2:15 today. So I encourage us to use the benefit of

his expertise and knowledge for any questions that you may have today. Thank you. I would like to now introduce Mr. Worrell.

MR. WORRELL: Good morning, Mr. Chairman, and distinguished panel members. My name is David Worrell, and I am the senior regulatory affairs specialist for American Medical Systems.

Before I proceed with the indication and the device information, I would like to state that the device has undergone extensive pre-clinical testing to demonstrate that it functions as intended. The device shares materials and operating principles with a similar device manufactured by American Medical Systems, the AMS Sphincter 800.

The AMS 800 has been legally marketed for 28 years, and has been used to treat urinary incontinence in over 50,000 patients. In September of 1999, the FDA approved the commercialization of the Acticon Neosphincter in the Humanitarian Device Exemption.

The approval recognized that the device is safe for use in patients, and that the probable

benefits outweighed the risks associated with the use of the device. The HDE approval also demonstrated that device design, functionality, biocompatability, and sterility, have been demonstrated.

Now I will proceed with the indication for use and the device information. Fecal incontinence is a distressing and isolating condition. As we heard during the public presentation, fecal incontinence dramatically impacts the emotional, social, and work-related aspects of a person's life.

Fecal incontinence presents a range of severity, severe or end-stage fecal incontinence, means the involuntary loss of solid or liquid stool on a frequent basis, and frequent used here means in the kinds of episodes that occur daily, or more than once a week.

Patients with severe fecal incontinence form a subpopulation from patients with fecal incontinence. Mild cases of fecal incontinence can be successfully managed with medical therapy, including anti-diarrheals, bulk laxatives, and biofeedback training.

With good compliances, these therapies produce acceptable results in mild cases. However, in general, these therapies are not very effective for moderate to severe cases of fecal incontinence due to neurogenic or traumatic origins.

Surgical treatment can benefit selected patients. Overlapping sphinctoplasty is a procedure of choice for an isolated anal sphincter defect, improving the health between 60 to 70 percent of these patients.

Post-anal pelvic flow repair has been advocated for significant occult sphincter defects. However, long-term results from this procedure have been disappointing.

If a patient fails these treatments, or if their physician thinks that their chances of success are not good using these treatments, the Acticon offers an additional option instead of permanent stoma.

The Acticon is used to treat severe fecal incontinence in post-pubescent males and females who have failed, or who are not candidates for, less

invasive forms of restorative therapy.

Fecal incontinence itself is not rare. "The true community prevalence of fecal incontinence is unknown," concluded colorectal surgeon, Dr. Robert Matoff in a recent report. Part of the reason for this is that many people fail to report fecal incontinence to their physicians.

The literature reports that the prevalence of fecal incontinence ranges from 2.2 to 7.1 percent in the general population. This means that about 5-1/2 to 18 million persons suffer from some degree of fecal incontinence.

The prevalence of severe incontinence is conservatively estimated at less than 170,000 persons in the United States, between the ages of 18 and 65 years old.

In 1996, AMS received FDA approval to begin its pivotal IDE clinical trial, with a device designed specifically to treat severe fecal incontinence, using the same materials and operating principles as the AMS 800 urinary sphincter, the new Acticon Neosphincter featured a reinforced cuff tab,

increased cuff widths and lengths, higher balloon pressure ranges, and larger balloon volumes.

The modifications were intended to create a device more suitable for the higher pressures encountered in the anal canal, versus the urethra, and a cuff more compatible for implant around the anus. Also in 1996, the Acticon was CE marked and European distribution began.

Today, the device is sold in over 30 countries, including Australia, Brazil, Canada, China, Israel, and the European Union, and about 1,000 devices have been distributed so far.

Here you will see a photograph of the Acticon Neosphincter. At the top of the photograph, you will see the pressure regulation balloon, and at the bottom of the photograph, you will see the control pump, and in the middle of the photograph is the cuff that encircles the anus.

From the pump to the pressure regulating balloon is kink resistant tubing that is color-coded black, and from the pump to the cuff is kink resistant tubing that is color-coded clear.

In this line drawing on the left, you will see a side view of the pump, and this is the kink-resistant tubing on the left there that is color-coded black, that goes to the balloon; and this is the kink-resistant tubing color-coded clear that runs to the cuff.

And this is what is of interest in this line drawing right here. What is not noticeable in the photograph, but is seen clearly right here, this is the cuff shell. As fluid enters the cuff, this cuff shell inflates, and as fluid leaves the cuff, this cuff shell deflates.

To defecate, the patient squeezes and releases the lower soft part of the pump several times. This causes the fluid to move out of the cuff and into the pressure relating balloon, and that is demonstrated in the line drawing here.

When the patient squeezes the pump, the fluid leaves the cuff, and moves through the pump, and into the pressure regulating balloon. As the fluid leaves the cuff, the cuff opens and removes the occluding pressure on the anal canal.

And the anal canal opens, allowing stool to pass through the anal canal and leave the body. Pressure from the balloon automatically returns fluid through the pump to the cuff, and after several minutes, the cuff closes and continence is restored in the patient.

At this time, I would like to introduce Dr. Doug Wong. Doug Wong is our principal study investigator. He has participated in two studies with the device, and he will present the effectiveness results from the study.

DR. WONG: Thanks very much, David. Good morning, Mr. Chairman, and Panel Members, my name is Doug Wong, and I am the Chief of Colorectal Surgery at Memorial Sloan-Kettering Cancer Center. I do not have any financial interests in American Medical Systems, apart from being a study investigator.

I am pleased to present the effectiveness portion of this presentation this morning of a device that I believe really does offer us a device that is safe and effective for the treatment of end-stage fecal incontinence for patients so afflicted.

I was a principal investigator for the pilot study and initial IDE in 1988, and also for this study that began in 1997. And in the presentation, I am going to give you an overview of the device implantation, as well as the effectiveness of the device in this particular study.

This is the Acticon device that is implanted, both in males and in females. It is a 3-piece device that is comprised of a cuff, a control pump, and a pressure regulating balloon. So the first aspect of the operation is to implant the cuff around the anus.

We size the cuff with a little sizer to tell us what the appropriate size is. The implantation is made by making a tunnel around the anal canal, and then the control pump is placed in the scrotum in the male, and in the labium majora in the female.

And then a pressure radiating balloon is placed in the space arestis in that area there, and then there is a connection tubing that connects all three components, and it can be regulated.

The patient can control the regulation as Mr. Worrell demonstrated, and at the end of the implantation, we cycle the device, and then we deactivate it with that little deactivation button and leave it deactivated for about 6 to 8 weeks after implementation.

The actual operating time takes approximately 90 minutes for an implantation. Our study was a multi-center prospective, non-randomized study, in which patients served as their own controls. It was conducted under a common protocol, and the end points were measured at pre-implantation, at 6 months, and at 12 months, post-activation.

Our inclusion criteria were patients with fecal incontinence, who had had at least one non-surgical attempt at treatment prior to, and the exclusion criteria included patients with Croyns Disease, patients who had had irritable bowel syndrome, as the only ideology, or the only potential ideology of their incontinence, and patients who had extensive pelvic radiation were excluded from the trial.

There are 19 clinical sites for implantation; 13 in the United States, and 3 in Canada, and 3 in Europe. The numbers documented in the brackets represent the proportion of patients that were performed in each of these global sites.

And 115 patients were initially enrolled in the study, and three of the patients had to be aborted during the surgery because of interoperative complications, generally a perforation of a scarred area, usually in the vagina or in the rectum.

So that left us with 112 patients that we implanted with the device, and you can see that the majority of patients are female, which those on the panel will recognize as being the commonest group that has problems with incontinence.

And the mean age is 49, with a duration of incontinence, a mean duration of incontinence of some 14 years. The etiology of the incontinence in the study population is listed here.

The obstetric injuries were the leading cause of injury, and then the other causes in the next three are pretty evenly distributed between neurogenic

incontinence, congenital etiologies, and anorectal trauma.

The other indications are listed at the bottom and comprise some 14 patients, and there were 3 patients with rectal prolapse, and 3 with endopathic incontinence. One was radiation injury, and one other with miscellaneous causes.

Now, virtually all patients had significant treatment by other modalities during the course of their management. All patients really had a long history of fecal incontinence.

Many had tried medical therapies and the majority had had previous surgical attempts at repair, all of whom had failed conventional treatment. And 38 patients, in fact, had previous sphincteroplasties listed there, and in fact of those 38 patients, 10 had had multiple attempts at sphincter repair surgically and had failed multiple attempts.

And 30 patients had a stoma or preexisting stoma at some point in time in an attempt to manage their fecal incontinence; and five had failed the dynamic graciloplasty procedure, and were then entered

in the Acticon trial.

So really this surgical procedure now is really a last resort for this patients, and they are going to have severe end-stage fecal incontinence once they have failed conventional management, often many times over.

CHAIRMAN KALLOO: Did you have any patients who did not have conventional management?

DR. WONG: And they all had conventional management. So had -- they had all failed conventional medical management, and the majority of patients had surgical attempts that failed.

The ones that had no potential option for surgery, like the neurogenic incontinence, there is no appropriate surgical procedure. They had all failed medical management, including biofeedback, bowel management regimes, changing things.

The primary end-point for the study was the fecal incontinent scoring system, which we will discuss in a moment. This would take place at pre-implant, at 6 months, and at 12 months.

It was a statistical comparison of the

pre-implant, and the 12 month fecal incontinence scoring system. The second end-points for the study were a measurement of anal manometry, a health status questionnaire, and a fecal incontinence quality of life questionnaire.

Now, this is the fecal incontinence scoring system, and which is referred to as FISS. This was developed by a small group of investigators and the sponsor of the study. This was specifically designed for this study, and specifically designed for fecal incontinence.

And it consisted of a five item, self-administered, questionnaire that patients filled out. The scores, as you can see, range from zero to 120. A score of zero is a patient who is fully continent, and a score of 120 is a patient is incontinence to liquid or solid stool on a more than once a day basis.

Eligibility criteria for the study was a score equal to or greater than 88, meaning the patients were incontinent to liquids or solids on a more than weekly basis.

The success rate was defined as a 24 point

drop from FISS levels. So a two component drop constituted a success for study criterion.

DR. EPSTEIN: Dr. Wong, can I ask you -- can you go back one slide, please.

DR. WONG: Sure.

DR. EPSTEIN: What is the difference between, let's say, a 73 and a 84, and where does the range come in?

DR. WONG: The fecal incontinence scoring system had -- there were five questions, basically stated, are you incontinent of gas, and each had a score. and incontinent of liquids, and there was a series of scores, and then the fifth question was a quality life score that gave five points for quality of life effectiveness.

If quality of life was not affected at all, then it was zero. If your quality of life was affected it was five. So it was a cumulative of those five questions, and so there is a range that represents the scores.

These are the matched fecal incontinence scores. On the left-hand side, you will see the six

month data, and the pre-implant mean fecal incontinence score was 106. You will remember that 120 is maximum.

As you can see, at six months at the follow-up fecal incontinence score, they are given the same questionnaire at six months. You can see that their mean score at six months had dropped 56 points to 50, and by the 24 point criteria of success is an 81 percent success rate in those patients that had functioning devices.

At the 12 month follow-up, a very similar picture. We now have again a mean incontinence score prior to implantation of 106, and which fell to 49 at 12 months, and that has maintained over that period of time, and again represents a significant reduction in the mean score.

And in fact this average point drop is in fact twice the 24 that we consider a success by the criteria that were done. Some of these average patients then who had then improved by that magnitude of a drop really went from an average incontinence of at least being incontinent once a day, to being

incontinent of seepage only based on that scoring system that I presented to you.

This was statistically significant to the P value of .001, and I think that it does show that the primary end-point for the study, in terms of effectiveness, was met. Now, I think that all --

CHAIRMAN KALLOO: Do you have a simply quality of life, because if you are able to reduce the scores from a statistically significant amount, in terms of just leakage, do the patients still have to wear underwear and all that. And do you have or have you isolated just quality of life scores?

DR. WONG: Well, we have quality of life data that I will present, in terms of the fecal incontinent quality of life score, and it wasn't a scoring system that we went with based on percentages.

And so actually a specific analysis was not done on that. There is a specific analysis done on the health status questionnaire on patients prior to and after.

But the data on the fecal incontinence quality of life I will present. I think that all

treatments for fecal incontinence should be evaluated on an intent to treat basis, and I would just like to take you through this intent to treat status line.

So we enrolled 115 patients, and 78 have implanted devices, and 3 were aborted, and 34 were explanted, and that will be discussed later in the safety regulation or safety presentation.

So we have 75 functioning sphincters that we know about, and three have been lost to follow-up in the study. Now, of these 75, seven had preexisting stomas. If they had a preexisting stoma, you can't determine their pre-operative incontinent status on the fecal incontinence scoring system, because they don't have bowel incontinuity.

And 68 were done without stomas, and so these ones that had preexisting stomas, we assigned or we felt that they had surgery, and had a stoma applied, I think it is fair to success that their mean incontinent score is probably equal to the mean of the study participants who did not have stomas.

So we applied that same mean in order to calculate whether it was success or not. One has not

reached a one-year follow-up in the stoma patients; and five in the patients done without stomas have not yet reached the one-year follow-up.

We really have six stomas and 63 non-stoma patients who were seemed successful based on that 24 point drop. So we have 59 successes, and I felt that it was fair to exclude those, even on an intent to treat basis, as they are lost to follow-up, and have not reached one year follow-ups. I really don't know what their follow-up is.

So on an intent to treat basis, 59 successes out of the 106 for an intent to treat basis, a success rate of 56 percent. If you look at the clinical successes, and the score at 12 months in that matched data that I showed you a couple of minutes ago, was 85 percent. The intent to treat success rate here is 56 percent. So we can see that patients who do retain a functioning device, the success rate or device is actually very successful in controlling their incontinence.

And even on an intent to treat basis, we have a 56 percent success rate with the study. And I

think we should put that into perspective. Again, we are talking about patients who are looking at a last resort for their fecal incontinence.

That list of operative procedures that I listed for you previously included patients or I listed sphinctoplasty, and patients with post-anal repair, and who have anterior and a posterior post-anal repair.

And if you critically look at the literature, with the success rates for those particular operative procedures, which are mainline procedures for treating people with incontinence, the success rate overall is very similar to this.

At our Society meeting just this past June, there were two papers that were presented, in terms of sphincteroplasty, which is the commonest operative procedure we do for restoring incontinence, and the long term results were in the 50 to 60 percent range with the conventional mainstream patients.

These are patients who have already been down that road, and we still have an intention to treat success rate of 56 percent.

Anorectal manometry was a secondary end-point in the study, and you can see that at pre-implantation the average resting pressure was 26 in this group of patients.

You can see that after implantation we increased the resting pressure in these patients at activation to 47 millimeters of mercury, and it has pretty much stayed very stable over the course of this follow-up on this study population.

And again, a pre, compared to 12 month, anorectal manometry score is again specifically significant. So that the secondary end-point, in terms of anorectal manometry again has been met.

The health status questionnaire was developed by the Health Outcomes Institute. This is a validated questionnaire. It is a 39 item self-administered instrument. It is based on the SF-36 and MOS-20.

And it really measures eight domains of health, and these eight domains include health perception, physical functioning, role limitations, role limitations in terms of physical functioning, as

well as emotional functioning; and social functioning, mental health, pain, and energy levels.

The scale is from zero to 100, where 100 is ideal functioning, and the total health status questionnaire adds the scores from each of these eight domains. This was given to patients at pre-implant, and again at 12 months, and here are the cumulative scores.

And again you add all the scores in those eight domains, and pre-implant compared to post-implant, in terms of the health status questionnaire. Again, a significant improvement with the implantation of the device.

And these are the eight domains listed. You can see that in each of the eight domains there was improvement, again with 100 being the ideal functioning. So there is improvement in each of the 12 month scores, compared to pre-implant.

And 6 of these 8 were statistically significant. with emotional problems and pain not quite reaching statistical significance. So in terms of the health status, again the secondary end-point

for the study was met.

The fecal incontinence scoring system was specifically designed for this study, and it is a 39 item, self-administered, instrument. And this was developed by the investigators and by the sponsor of the study.

And this led to the 29 item instrument that was validated subsequently by the American Society of Colon and Rectal Surgeons Outcome Group. It measures the physical, psychological, and the social impact of fecal incontinence.

The reported rates are really in percentages, and are listed in these subsequent slides. You can see that for physical functioning that in the blue bars we have the pre-implant.

And you can see that 42 percent of patients avoided certain foods, and 34 percent used medications, and 42 percent prior to implantation used diapers; and 77 percent used pads on a regular basis.

And you can see that after implant, at a 12 month review, only 9 percent altered their diet significantly. And 27 percent of patients still used

some medications, but only 9 percent needed to use diapers, and 39 percent still used some form of protective pads.

And 81 percent, as Nancy Loitz told you this morning, it is very common that patients will look for where all the bathrooms are, and stay very near a bathroom. And 81 percent in the study prior to implantation sought out where the bathrooms were, and stayed very near them when they left home.

After the implantation, only 33 percent felt the need to do this. And 47 percent leaked stool unknowingly, and 57 percent couldn't hold the bowel movement long enough to make it to a bathroom; and 89 percent I had a feeling that they could not control their bowel movements.

And again you can see very dramatic improvements in these percentages when we look at the post-implant, 12 month review, of these aspects.

DR. KOLTUN: I assume that all this data was handled in the same way, and that your post-implant data was presumably on the successful patients, and the 50 percent figure; and the pre-

implant data is the full 115?

DR. WONG: That's correct.

DR. KOLTUN: Did you look at this matched?

DR. WONG: No, we did not look at the matched data, in terms of the -- well, these are just patients that have a functioning sphincter.

DR. KOLTUN: And my next question is when it came to quality of life issues, such as this, social functioning, why couldn't you have assessed the social functioning and included those patients who felt they may have ended up worse?

DR. WONG: Well, this was administered to -- well, at least the fecal incontinence quality of life was administered to all study representatives.

DR. KOLTUN: And this includes all the patients?

DR. WONG: This includes all the patients in the study, correct.

DR. KOLTUN: Pre-and-post?

DR. WONG: That's right.

DR. KOLTUN: And those who failed?

DR. WONG: That's right, but we did not

statistically compare the results of this. It is hard to apply a score to this, and this is the percentage of patients who responded to these, but did include patients who actually had -- any patient who had the device implanted, and had functioning devices, whether they were successful or not, were included in this.

CHAIRMAN KALLOO: Do you have the same data beyond 12 months? Have you looked at it at 24 months?

DR. WONG: We have not yet by this point in time. There are not many patients that have reached the 24 month point yet. Again, in terms of social functioning, 83 percent were not able to make it to a bathroom, and 64 percent planned their schedules around bowel movements.

And 81 percent who went away stayed near a bathroom, and 69 percent avoided wearing light clothes because of the fear of having an accident and it being evident.

After the implantation, the results are 21 percent, 21, 33, and 24. Again, a significant improvement clinically.

MS. NEWMAN: I just want to make sure that I am clear on this. So this is the matched groups pre-and-post?

DR. WONG: These are patients, all the patients.

MS. NEWMAN: And all the ones -- and it doesn't matter what happened with them?

DR. WONG: All the ones that had a functioning device.

MS. NEWMAN: So the red is only the individuals that had a functioning device?

DR. WONG: That's correct.

MS. NEWMAN: And you did not match those with their pre-scores?

DR. WONG: These were not.

DR. KOLTUN: So the end of the blue is 112, and the end of the red is 60 something?

DR. WONG: At 12 months, 67, right. In terms of psychological functioning, 48 percent considered their job more difficult; and 76 percent worried about odor; and 86 percent worried about accidents; and 68 percent said they could not do many

things that they would otherwise want to do.

And again the red bars are those having functioning devices at 12 months, and there was improvement. So I think the primary objectives of the study clearly were to assess incontinence before and after activation of the device.

The primary end-points, in terms of effectiveness, showed significant improvement at 6 and at 12 months. And the primary end-point was met, and the secondary end-points, in terms of improvement and quality of life in these patients, likewise as well as the anorectal manometry, did show that the secondary end-points were met.

So I think based on the study that it is fair to say that the patients who do have a functioning device can significantly have improved continence, and that they do have a greatly enhanced patient quality of life if they are able to have a functioning device at the end of the study.

So I thank you for your attention, and I would like to turn the podium over now to --

CHAIRMAN KALLOO: First, are there any

questions?

DR. WOODS: I am specifically interested in a little bit more on sub-group analysis, and the main question is that when you look at the FISS scores, there appear to be three groups of patients that would have qualified to enter into this study according to a three point score analysis.

And those are those that had greater than weekly, and those who had daily, or those that had more than daily episodes of incontinence.

DR. WONG: Yes.

DR. WOODS: Did you look at the data according to those sub-groups to see whether or not the most severe and the least severe within those groups were more likely to respond; and where the point drops more dramatic in one group than in the other.

DR. WONG: I would ask one of the statisticians to address that if they would. Mark.

MR. ANTIL: My name is Mark Antil, and I am the biostatistician for American Medical. We didn't break them down into sub-categories by what

their score was pre-versus-post.

What was presented here was an overall mean drop across time, basically looking at the pre-implant, the 6 month, and then the 12 month, and that is how we analyzed it.

DR. WOODS: I am really interested in knowing whether there are certain patients that may be more likely to respond, and should we tell those with the most severe fecal incontinence -- you know, a patient with a score of 120 -- that they may be less likely to have a good outcome than those who have --

MR. ANTIL: I understand your question.

DR. WOODS: -- a lower score, and also with respect to ideology of their --

MR. ANTIL: Yes, we did do a sub-group analysis by etiology, which we listed for the obstetric, neurological, and so on. There was no statistical difference for the HSQ or the FISS scores between those 4 or 5 groups.

Also, we looked at those for explants, and revision rates, and those were not different also with the long range tests. So we did look at a number of

sub-group analysis, and they did not indicate a difference there.

But again going back, we did not categorize these by if you had a higher score to begin with or not. But the average score of most of this overall group, and I believe it was over a hundred, a 102 or so, of the FISS score. So they did all start off pretty high to begin with, but we did not break them down.

CHAIRMAN KALLOO: My question is that you started this pilot study in 1988, and it seems to have taken one hell of a long time to get it together and put it all forward. And I just wondered is that because of some lack of enthusiasm on your part?

And the other question that follows that naturally is that you have 19 sites, and out of the 19 sites, you only gathered 118 patients. Why is that so limited?

DR. WONG: Those are excellent questions. You are right. The pilot study was done in 1988, and it was not because of a lack of enthusiasm on our part. We were very excited about the results of the

initial pilot study, and we are very anxious to actually proceed.

I am talking about study investigators when I was at the University of Minnesota. There was a decision by American Medical Systems at that time that held up proceeding with the use of the device for fecal incontinence. So it was not until 1997 that we were able to move forward with what we felt was a very promising device for this problem.

And someone from American Medical Systems may want to address that question separately as well. I'm sorry, but your second question was?

CHAIRMAN KALLOO: The 19 sites and the approval is so small.

DR. WONG: Well, these again were in-stage fecal incontinence patients. It did take time to accrue those patients. There was training that each of the sites needed to go through.

There are a lot of patients that present for fecal incontinence, and there are a lot of potential mainstream treatments that these patients need to have and to go through in order to make sure

that all other avenues have been addressed.

And so, yes, it did take a period of time to accrue those patients. And again we have limited it to really quite in-stage frequent incontinence.

DR. KOLTUN: I have a question, but I guess you are talking about the effectiveness, and my question relates to safety, but also as to the data that you have here.

And that specifically is that when I look at the FISS score, there is -- let's say there is a score of 84, and the patient is incontinent to liquids or solids, more often than monthly, but not as often as weekly. Could such a patient be in the study?

DR. WONG: I don't know. Well, was the 88 equal to or greater than 88 was the score?

DR. KOLTUN: The patient would have to be incontinent to liquids or stools more often than weekly.

DR. WONG: Okay.

DR. KOLTUN: But not more often than daily.

DR. WONG: That's correct.

DR. KOLTUN: I am asking what happened to those patients in that category who were not of the worst incontinence if they failed? What was their subsequent incontinence, and in fact did you make them worse?

DR. WONG: Did we make them worse by incontinence?

DR. KOLTUN: Yes, after going through the procedure.

DR. WONG: I haven't got specific data that I can give you antidotal experiences and things that the patients -- even the patients that were incontinent to that level that were facing or having a device done as a last resort.

And from my own experience, when I meet with those patients, I basically tell them -- and we have discussed -- the next step in their incontinence is a colostomy or a stoma.

And that is the same group of patients that have a score of 88, and if their quality of life is so affected that they would agree that if they were to fail this device that they would have a stoma, then

I would consider them a potential candidate for that.

So I don't have any evidence that we made any patient worse that failed, but some of those patients that did fail went on to have a stoma at the time of explanation because we knew that their incontinence was such that they were facing that decision is it this, or is it a stoma at that point in time.

CHAIRMAN KALLOO: I have a question, and I am not sure that you can answer it, but obviously there has been a tremendous or lots of experience in Europe, where this device has been obviously inserted in many more patients. Do you have any data on the effectiveness of the European experience?

DR. WONG: Well, from the published experience, the success rates have been generally in about the 80 percent range, and their morbidity rate is somewhat lower than with this study.

Those tend to be in centers where one investigator has been doing the implants, and has far more experience than what we can bring to bear in a 19 center study, where some people only do 2 or 3

implants over the course of things. But the success rate has been good.

DR. MCCLANE: To follow up on that, were there any centers where the success was better than in other centers in the study?

DR. WONG: Again, I would ask Mark. I don't believe that there was any difference in the things. Again, pretty small numbers to be making any statistical statement of that. I don't believe there is a difference. Mark.

MR. ANTIL: We did test the pre-scores to look for site differences, and they were not statistically different, but the numbers were pretty small for some of the sites. So we didn't evaluate them on a post-by-site difference. So we didn't evaluate that.

DR. MCCLANE: And my other question is I assume now that the patients with the colostomy have had -- well, is that something that has been considered?

DR. WONG: That was not part of the initial trial. They did something that I am

personally interested in pursuing with this device at some point, but that was not part of the study.

MS. NEWMAN: Well, in the urinary field, we have this sphincter, but in women it is not really used in this fashion. What is your views on this, on male versus female?

DR. WONG: Well, I think that when we put the -- well, the integral part of this procedure is the placement of the cuff, and --

MS. NEWMAN: Well, no, it was really the balloon, and dealing with erosions, and those things.

DR. WONG: You mean the pump, of the pump, and not the balloon?

MS. NEWMAN: Right, the pump.

DR. WONG: In terms of -- or in our setting, basically it has been the cuff that has been the main anatomic difference, in terms of things. We have had some infections in the labia, but that has not been a major difference between putting it in the scrotum and the labium.

Most of the anatomical differences have been in trying to get that tunnel between the vagina

and the rectum in female patients, particularly having a child birth injury, with a scarred perineum. So the cuff placement has been more of an anatomical sex difference between males and females.

MS. NEWMAN: Maybe there are better surgeons in your offices?

DR. WONG: I wouldn't want to say that.

CHAIRMAN KALLOO: Okay. Thank you.

DR. WONG: Thank you.

DR. CONGILOSI: Good morning, Mr. Chairman, and distinguished panel members, my name is Susan Congilosi, and I am a study investigator. And I am pleased to report on the safety results for this device. I have no financial interest in American Medical Systems other than that of an investigator.

I am going to review this in terms of two safety objectives; first looking at adverse events associated with the actual implant of the device, and then adverse events that occurred after implantation of the device.

There were 15 adverse events that occurred at implant. As you can see at the bottom, the

majority of these involved in perorations to the vagina or the rectum at the time of implantation.

As Dr. Wong just pointed out, a number of these patients have a scarred and fragile perineum, and the actual surgical procedure of performing blunt tunnels around the anal canal can be technically difficult, particularly in these scarred patients. If a perforation to the rectum occurred, we did not go on to the placement of the device.

And if a perforation of the vagina occurred, we would repair the device and would go on to placement and were successful in that venue. All of these injuries were identified at the time of surgery and repaired, and going on as I stated, not placing a device if the rectum is perforated, and going on if the vagina was, and all resolved without long term sequelae.

These other two adverse events occurred at the time of removal of devices. The remaining adverse events involved those that occurred after implantation of the device.

There were no deaths, no life-threatening

events, and no unanticipated adverse events in this study. There were a total of 395 adverse events, approximately half of which were thought to be device related.

This is a list of the more common adverse events that occurred in at least 10 patients. These events are not mutually exclusive. A patient may have had more than one event, and there may be multiple events for any one patient, and multiple interventions for any one event.

For example, a patient who presented with a mechanical malfunction may also have been reporting recurrent fecal incontinence. A patient with constipation and impaction may also have been reporting pain and discomfort. A patient with pain, discomfort, infection, and erosion were often reported together.

DR. TALAMINI: Dr. Congilosi, can I ask a question? The infections I am particularly interested in, because obviously in this region an infection can be all the way from mild, requiring some antibiotics to necrotizing fascitis.

Can you give us some more details on what these infections entailed, and how they were treated?

DR. CONGILOSI: I will go into more detail on the infection, but I will make brief comments now that in general the majority -- well, I think the number of infections were 36, eight of which we could treat just with antibiotics.

The other ones went on to explanation of the device. So, yes, infection and erosion is usually the reason that we had to explant the device. But these patients would often present with critical symptoms of pain, a small amount of bleeding, change in drainage, and possibly near fecal incontinence.

There were no patients with necrotizing infections. We would go on to explant these devices, and usually it was a hospital stay of 1, 2, or 3 days; a day of P/O antibiotics, and then oral antibiotics for a week.

Wounds were left open in the perineum if they had eroded, and in my experience all of these would heal quickly over several weeks. So, no necrotizing infections, but septic admissions for

this.

DR. TALAMINI: And going back to the previous point. Were any of those patients reattempted at implantation, or on the other hand, had to go quickly to an ostomy?

Do we have more information on what happened to that group that had infection and implantation, and whether we made them worse by having tried to put this in and wound up with an infection?

DR. CONGILOSI: Again, in that group, as Dr. Wong said, a number of these did go on to reimplantations and some successful, and I can ask to be given the exact numbers on that again.

But some chose not to go on to reimplantation, and again were a group that would go on to a stoma because that had been the decision prior to surgery that that was their last option.

DR. TALAMINI: Thanks. I think that is a key thing that many of us are thinking about, did we make people worse by trying this, and I think you will probably hear that question a few times.

DR. CONGILOSI: Our counseling of these

patients, I think you probably got that sense from Doug that at the University of Minnesota, because we have implanted more of these, we get a lot of patients referred from out-of-State and out-of-country.

And we do not go on and implant all these patients. I actually insist that they come up for an initial meeting with no plans for surgery, although many would like to have surgery, combined with an out-of-town trip, because we found that a number of these patients are amenable to other procedures.

We redo all their physiology testing, and if they are still a candidate for another surgical procedure, or another treatment, we do that. These are truly our end-stage patients, and we certainly have refused a large number, and had them go on to other treatments.

And if they were then unsuccessful, then to advise us, because a stoma was their last point. Again, this reflects at least 10 patients in each group, and these are not again mutually exclusively, and many of them are multiple --

DR. MCCLANE: Do you know what percentage

of patients have had an adverse event? Did some get through with no events, or do you have anything on that data?

DR. CONGILOSI: Well, 100 patients had adverse events.

DR. MCCLANE: So 100 out of 115? So, 15 didn't?

DR. CONGILOSI: Yes.

DR. EPSTEIN: A question. Was the erosion -- well, going back, was it mostly the pump that was eroding, or --

DR. CONGILOSI: I will get to that in further slides. Yes, a like number of patients had adverse effects, but the majority of these were mild and moderate. Severe was termed an adverse event that prevented a patient from continuing with their daily activities.

The majority of the adverse events did not require surgical intervention, and 17 percent required no intervention. Reflective of this would be someone complaining of constipation, and even without medical management it resolves.

Or early complaints of pain after the device has been activated, but does resolve with time. An examination of the patients who would be treated medically, it would be possibly some variation in bowel regimen, and constipation was an issue for some patients.

And surprisingly, they would sometimes have to be placed on laxatives. My routine post-operative instructions to these patients were to stop all the anti-diarrheals which they were used to for years of using, so that we could see what their function was like, because many were still very nervous about not talking those usual medications, and would develop constipation.

And not evasive intervention. Let me think. Well, I can add some if you want more clarification on that. Well, 36 percent had surgical intervention for these adverse events. So there are 142 adverse events that required surgical intervention.

Again, remember that these aren't mutually exclusive. Many patients had several adverse events

that might be resolved by a single surgical procedure. And 60 patients underwent 101 procedures. There were 81 device revisions in 56 patients.

And 20 other ancillary procedures, and those ancillary procedures included disimpactions, and incision and drainage of would infection, implantation of a cuff sizer, or procedures like that.

DR. KOLTUN: What was that last phrase?

DR. CONGILOSI: Implantation of a cuff sizer.

DR. KOLTUN: And what is that?

DR. CONGILOSI: The sizer is what we use at the time of surgery to decide on the size of the cuff.

DR. SMITH: So why do you use that on implantation?

DR. CONGILOSI: Well, it is solely not recommended by the company, and very discouraged, and an investigator might have chose -- and I think this is on a very small number of patients, but that if they had a perforation to leave the sizer in to preserve the tunnel.

And if they didn't develop an infection, then go back and place a device. In many of these patients where there are very, very scarred and fragile parineums, we often feel that we probably have one good attempt to get a tunnel in this area.

And if we lose that attempt, we probably have lost the opportunity to provide them with this device.

DR. KOLTUN: I was going to ask this question about this device later, but since we are kind of on it, it seems as if there are many sizes. There are different sizes of balloons --

DR. CONGILOSI: From 8 to 14 centimeters, the majority of which received sizes 10, 11, and 12.

DR. KOLTUN: And so my questions are two; one, how do you decide the sizes of each of those devices and the cuff; and, two, with the revisions, could the revisional surgery be minimized by improvement in that regard?

In other words, were some of these revisions simply because of choosing the wrong sized cuff, and if so, how do you do that?

DR. CONGILOSI: Okay. That is a very good question. There is a number of reasons for the revisional surgeries, but specifically regarding the cuff sizes, when we make the tunnels, we then put the sizer around and pull it to snug.

And I realize that is a vague term, snug, and it is probably the hardest thing to teach the new surgeons on how tight is tight enough. We actually went to placing them slightly looser later in our experience because we found that incontinence was not the problem if these were functioning successfully.

It was tending towards constipation. As Nancy told you, even where a cuff that had no fluid in it, she was having some element of control. So we went to slightly looser cuffs, and in that we may have seen more instances of tissue shrinkage, and then the cuff being on the loser side, and having to go back and place a tighter cuff.

But when I would do that, often the resizing of the cuff was two sizes down. We did not err two centimeters on the cuff. It really was tissue shrinkage. So some of this is an element of the

change in their anatomy with time.

This is probably going to be a little bit more likely in patients such as with a perforated anus, with even less muscle around the anal canal. The other issue is device revisions, and was a problem with the tab on the cuff for buttoning.

This was realizing that the tab was revised, and with a new tab, but that was not available during this study period. So if a cuff became unbuttoned, we would have to go in and replace the cuff in that instance.

DR. KOLTUN: So explain that process to me. In other words, you create a tunnel, and that is defined by the physical nature of the patient?

DR. CONGILOSI: Right. Incisions are made either two -- well, one on each side of the anal canal, or an anterior incision. In females with very thin parineums, we often might do an anterior incision because that plane would be so narrow, but there is no real difference between those two options and investigators use both.

DR. KOLTUN: And if you make your tunnel,

then what is this sizer? Are there different sized sizers, or is there just one sizer?

DR. CONGILOSI: There is one sizer with a small hole in it that you can pull the end through. I mean, sort of tighten it down.

DR. KOLTUN: Is that like a wire, or is it loose, or what?

DR. CONGILOSI: It is a silicon band, with a small hole in it. You pull the end of it through, and as you snug it down, it will read off the centimeter size.

DR. KOLTUN: And so that centimeter size read off that band then correlates with the cuff size that you use?

DR. CONGILOSI: Yes, the cuff size that we use.

DR. KOLTUN: So how often do you think cuff size was inappropriately chosen at the time of the initial surgery?

DR. CONGILOSI: I don't know how you would judge that.

DR. KOLTUN: How often did you have to

revise the prosthetic cup due to leakage or failure of control unassociated with infection, or --

DR. CONGILOSI: How many of those do we have for fecal incontinence or constipation? It would be those two categories.

DR. KOLTUN: Well, how technically demanding is this, and how much of the complications, which are obviously somewhat high, related to the technical nature of the procedure itself? That is what I am trying to get a feel for.

DR. CONGILOSI: Well, I will have them pull those numbers, but if it was simply because it was too tight or too loose, most of our revisions -- and I will refer to another slide here, where were there was a pump malfunction, or cuff openings, or component malfunction.

DR. KOLTUN: So it wasn't frequent that you had to go back because the cuff did not --

DR. CONGILOSI: No, it was not frequent for pure incontinence because the cuff was too loose, or pure constipation because it was too tight. As far as resolution of these events, 91 percent of them are

resolved, and there are 37 or 9 percent are continuing events, the majority of which are mild and moderate.

This was three severe events, and that are unresolved. The one was where the patient had fecal impaction, and was at a loss to follow up. The other patient was explanted and exited from the study, but did not return to see the investigator, and therefore could not be technically exited. And the third patient had rectal pain, which did resolve, but after the closure of the study.

DR. KOLTUN: A quick question. How does this compare in terms of the frequency of adverse events to the urinary sphincter?

DR. CONGILOSI: I don't personally place the urinary sphincter. Obviously the infection rate is certainly higher, and my sense is that the revisions are probably also higher involving the technical difficulty of working on the anal canal on these patients.

But I do not place the urinary device. We had -- you had asked about revisions. There are 81 device revisions in 56 patients. The vast majority

were revised once, but a number of patients did go on to multiple revisions.

I think this speaks to two things. One is the willingness of these patients to undergo repeat revisions, particularly if they have a functioning device, and a component is not working, or if there is migration of the pump.

It also speaks towards the minor nature of some of the revisions, again often involving overnight hospital stay, and more morbidity. Six of these revisions have to do with staging explants. If a patient presents with erosion in the perineum of the cuff, the cuff can often just easily be explanted right in the office.

And where removal of the pump in the labia, or the scrotum, and the reservoir balloon, does involve an operative procedure in a hospital. So that is why six of these involved two procedures.

This gets into why we have the device revision, and so I can explain a little bit more about your questions about cuff sizing. The majority obviously were due to infection or erosion.

These are reasons that would commonly lead to total explanation of the device. The other etiologies are those that would be the patient is undergoing partial revision, or a changing of a component, and these often led to patients retaining a functioning device.

DR. KOLTUN: I'm confused. The device revision to me means you fixed it and left it in. Wouldn't you have an infection or erosion and therefore an explant?

DR. CONGILOSI: Right. So for a patient with reoccurring incontinence, again these are not mutually exclusive, and so with an infection or erosion could also have reoccurring incontinence. So that is why it is a little difficult to pull out with pure incontinence and pure constipation.

Something like mal-position would be a pump in the labia that is in an uncomfortable position, and migration, the same thing. Possibly a pump that has moved higher in the scrotum or labia is harder to access, and that would be a revision possibly of just that component, where again these

would be full explanations of the device.

Regarding the erosions, there are 27 erosions that occurred in 24 patients. Not surprisingly, the majority of our erosions were to the cuff, the rectum, and the perineum.

Again, this reflects forming a blunt tunnel around the anal canal in patients that have previously often been operated in this area, and the area is scarred and fragile.

There were four that were of the pump; two in the scrotum, and two in the labia. And one of the two being in the perineal skin. And 47 pre-implant and implant variables were analyzed to determine possible factors that could be associated with the risk of erosion, and these were the significant events of which diabetes and preoperative musculoskeletal abnormalities were significant, and in a multi-variant analysis.

Musculoskeletal abnormality refers often to the trauma patients. An example of this would be a patient in a motor vehicle accident with a scarred perineum, and a patient who had a propeller injury,

and had had 19 prior operations for this.

And a gentleman who was caught in a trash compactor and had a hemipelvectomy. These are the type of multiple skeletal abnormalities of patients that we were operating on.

There were 36 patients who had infections in the study, and 30 infections were in these 28 patients who had device revision, and eight of the patients who had infections, their infections were resolved with antimicrobial therapy.

Most of the infections occurred early on. Remember that we were activating at 6 to 8 weeks, and so that is between that 30 and 60 day period. This led to the revision of our preoperative antimicrobial therapy, and I will get to that in a slightly later slide.

Again, those 47 factors were looked at for their significance for infection, and these list the significant factors. Again, preoperative musculoskeletal abnormalities stands out reflecting the trauma patients.

The preexisting stoma was a very small

number of patients, and this may be due to the low end. The majority of patients had a standard cuff width. So that also may reflect that factor.

DR. KOLTUN: Does that mean preexisting stoma increases your risk?

DR. CONGILOSI: Yes.

DR. KOLTUN: Why do you think that?

DR. CONGILOSI: Again, it was a very small number of patients that had --

DR. KOLTUN: You don't give these patients operating stomas?

DR. CONGILOSI: No, we don't. These are patients who presented to us with a stoma that had been placed because either after trauma, or they had been so incontinent that years earlier they had received a stoma. We did not routinely divert these patients for the procedure.

DR. KOLTUN: Well, if they had gotten their stoma for neuropathic incontinence due to diabetes, then maybe it wasn't the stoma, but was the preexisting illness of diabetes that you already showed was significant. I mean, I don't understand

that. I just don't understand the preexisting stoma.

DR. CONGILOSI: Well, the majority with preexisting stomas were not neurogenic patients. They were trauma patients usually.

DR. MCCLANE: Were they at the time of the implant, the stoma?

DR. CONGILOSI: No, the stomas would be -- we would implant the device, and we would wait until activation, and then if we could successfully activate, we would then the takedown the stoma.

So they did have two instances where they were at risk of infection of this device. One, when we put it in, and one with the takedown of the stoma.

DR. MCCLANE: And when you put it in, there was no stool device --

DR. CONGILOSI: Right. But still --

DR. TALAMINI: But on the other hand, they would have some diversion effects in their rectum, and some atrophy of --

DR. CONGILOSI: Yes, and there were certainly patients that had -- well, I personally, and this is antidotal, but I did personally have patients

that I perforated into their rectum, and have been diverted for many years, and aborted in patients with stomas.

DR. TALAMINI: I'm afraid that I am still not understanding the standard cuff width, and why that would be a risk for infection.

DR. CONGILOSI: The vast majority of patients had a standard cuff width used. I can't explain that.

MR. ANTIL: Maybe I can. Maybe I can either make it cloudy or clear on that question. But the univarian analysis is really an exploratory to look at the incidents rates.

Now, the multivaria looked at -- it is basically a log rank test to look in a forward fashion to see which factors up there might increase the risk of a revision.

Now, there may be an association, like what you were seeing with diabetes with the preexisting stoma, and for some reason that one came out versus the diabetes. So there could be an association with that.

DR. CONGILOSI: Okay. Regarding the infection rate, we obviously did notice this high rate of infections early in the course of this study. We therefore had this reviewed by an infectious disease specialist who looked at the organisms involved in the infection, which was a broad range of organisms.

But advised a new antibiotic regimen, which was then subsequently used in 16 patients. While this is not statistically significant, it certainly is clinically compelling, and we saw a drop in this infection rate from 27 percent to 12.5 percent.

DR. MCCLANE: And there were no antibiotics used in the first operation?

DR. CONGILOSI: Well, there were antibiotics used in the first operation, but those would usually be at the discretion of the investigator, and would reflect what a colorectal surgeon would typically use for an anorectal procedure.

And in particular I would say that the change often from this would be better coverage, and

in your package is the regimen, but for example, the addition of achromycin --

DR. KOLTUN: Was up to the --

DR. CONGILOSI: Actually, no. The antibiotic regime was a dose pre-op, and the early regime of two doses is post-op. It was the discretion if anything was carried on orally later on.

The antibiotic regime beforehand was similar in the amount, but it was actually just the change in the actual antibiotics.

DR. KOLTUN: Now, I don't understand. Your first comment says antibiotic regime not used.

DR. CONGILOSI: They got antibiotics, but it was the antibiotic regime that was advised by an infectious disease specialist.

DR. KOLTUN: In column one?

DR. CONGILOSI: In column two. In column one, an antibiotic was used, but not a specific regime that we later devised. So in the first column would be patients that had the device placed, and probably got, for example, sepitan and flagella in pre-op, or something like that.

We then advised a regime of different antibiotics and that was used in this 16 patients.

DR. MCCLANE: And did you look at the volume based on what antibiotics they got? Supposed they got no antibiotics? Did anyone not get antibiotics?

DR. CONGILOSI: They only looked at the two regimens. There were no patients on no antibiotics.

MS. BEAURLINE: We did prepare the use of antibiotics.

CHAIRMAN KALLOO: If you could please come up to the podium and state your name. Thank you.

MS. BEAURLINE: Diane Beaurline, American Medical Systems. We did analyses for use of -- well, if pre-operative antibiotics were used or not used, those groups were analyzed, and for infection on univarian analyses the P value was 0.1106, and so not significant. And again not significant on multivariet at 0.2615 being the P value in that instance.

DR. KOLTUN: And let me just say that nobody did not get any antibiotics. I thought

everybody got antibiotics.

MS. BEAURLINE: There were some patients who were reported to not receive pre-op antibiotics. The vast majority of patients did receive pre-operative antibiotics.

DR. KOLTUN: I am confused by this because a colorectal surgeon knows what the organisms are, and I am surprised to think that an infectious disease person couldn't improve upon that.

So it seems to me that the spectrum of organisms targeted by both of those antibiotic regimens, the first one being the colorectal specialist, and the second one being the infectious disease specialist, was probably very similar were they not? What were the antibiotics that we are talking about?

DR. CONGILOSI: Will you pull up the regimens?

MS. BEAURLINE: I have it here.

DR. TALAMINI: It kind of sounds like early in the study that there wasn't an antibiotic protocol.

DR. CONGILOSI: There was not a specific protocol.

DR. TALAMINI: And later there was.

DR. CONGILOSI: And later there was.

DR. TALAMINI: And in the early part of the study, that included some who neglected to give antibiotics on an occasional basis. So it really is just comparing a hodge-podge of whatever people gave to when --

DR. KOLTUN: A hodge-podge of colorectal surgeons' recommendations.

DR. TALAMINI: Correct.

DR. CONGILOSI: All right. This is the variety of microorganisms that were cultured, which as you can see is a long list, although the majority -- well, there is a wide variety here.

This was the recommendation for the infectious disease consultant, and not surprising, the infusion should be at zero to 60 minutes before incision, and that is a routine surgical recommendation.

This was the regimen that was recommended,

cefotetan and vanconycin. And this is the current one?

MS. BEAURLINE: Yes.

DR. CONGILOSI: The actual prior one was -- there was another one that was used in the study. This is the current one. The previous one was zosian and vanconycin. We actually weren't giving the cefotetan and what he recommended.

The cefotetan was often used, and again a hodge-podge, but he came back with a recommendation of -- I believe it was zosian and banko, which was the recommendation.

We have since modified it, and this is even a further modification, because one of the antibiotics he recommended if they were allergic was trovan, which is not on the market. This again goes on to allergies.

Therefore, in the current training of surgeons to do this, a number of factors do seem important to minimize the risk, and the antibiotic issue we have discussed. The use of a specific regime, and all patients get a full bowel prep, and

other things to limit infection in the operating room.

Patient counseling refers to those variables that we demonstrated with both infection and erosion that seem to indicate that some patients that are going to be at higher risk for this being unsuccessful.

Patients with diabetes, and patients with multiple traumas, and multiple perineum operations. That said, in our practice we would use this to counsel a patient, but not necessarily to refuse a patient based on those criteria, because again this is their last attempt at receiving continence, and they are a high risk group of patients.

Many of the patients in this study were very difficult patients for us to perform obviously, the musculoskeletal trauma patients, and patients with few other options, and stomas.

DR. GELLENS: I have a question. Do you have data on co-morbid conditions, like how many patients were hypertensive, or had diabetes, or vascular disease? Did you collect that data?

DR. CONGILOSI: Yes. Let me pull that

out.

CHAIRMAN KALLOO: While he is doing that, why don't you continue, please.

DR. CONGILOSI: Okay. Again, there were no deaths, and no life-threatening adverse events, and no one anticipated adverse events. The adverse events, while they appear numerous, were manageable, and could be resolved without long term sequelae.

And despite even requiring multiple revisions in some patients, a successful device could be achieved. And you heard that from Nancy today, because she is a patient who has undergone two placements of a device, and an infection, and there were no serious long term sequelae from the device revisions. Thank you.

CHAIRMAN KALLOO: I have a question before you go. Does this device preclude a -- if you have to do a colposcopy on these patients who have this device, and if so, are there special precautions?

DR. CONGILOSI: You deactivate the decide to do a colposcopy or a flexible sigmoidoscopy. You pump it open, and then you hit the deactivation button

on the pump. It is in their scrotum or their labia, and that locks it open.

You then perform the procedure, and then resqueeze the pump and that reactivates it.

DR. TALAMINI: If I could ask both you and Dr. Wong whether in this study did you have patients where the device was removed for patient dissatisfaction? Patients who just said I don't like this thing, and I would rather have a stoma, or I would rather go back to my previous state?

DR. CONGILOSI: Well, not pure patient dissatisfaction. There might be --

DR. TALAMINI: There were some revisions for dissatisfaction.

DR. CONGILOSI: Right.

DR. TALAMINI: But what about removals?

DR. CONGILOSI: Not for pure patient dissatisfaction. The other ones for dissatisfaction would have also been with people with recurrent fecal incontinence and dissatisfaction.

DR. EPSTEIN: I have a question, and again addressing Dr. Talamini's previous question. Were

there any cases of severe infections requiring prolonged hospitalization?

DR. CONGILOSI: No.

DR. EPSTEIN: You said that you believed that some of the wounds opened, and --

DR. CONGILOSI: Obviously, as someone who has put in a large number of these, and I have also taken out a large number of these, and I would routinely have them in the hospital a day, and then on oral antibiotics for a week, and the wounds would quickly heal.

And that includes the erosions. You know, rectum through to the vagina, which to a colorectal surgeon, a rectal-vagina fissel can be tremendously difficult to heal, and these would quickly heal.

DR. EPSTEIN: How do you define the outcome of the adverse events? In adverse events, you have erythema, fever, and abscess, and were organisms cultured?

DR. CONGILOSI: Organisms were not cultured at all in the removals for infection, and those would be signs of infection. Pain could be an

indication of infection, and we wouldn't realize that it was infection until we went to remove the device, and would find drainage.

Routinely, you would find drainage around the device, and that would be very clear, but there may be a few skin and external indications of the infection if they didn't have an erosion, or if they didn't have localized erythema.

DR. MCCLANE: There is a trend to look at the pelvic in women, which is an old time area, I know, in some specialties. Do you know anything about prolapse?

A large portion of your population was older, in the 50s or 60s. What do you think about that? What happens if they have a prolapse? It doesn't matter? Do you have inclusion or exclusion criteria?

DR. CONGILOSI: I actually see a number of those patients myself. I work with a urogynocologist and I am obviously familiar with that. If they had -- if there were some patients who would present with evidence of other prolapse, I would repair that first.

My worry then would be that might preclude having a successful device. Obviously, if having a vaginal prolapse, I am not going to put a cuff around the anal canal.

Some patients who -- and as Nancy pointed out, with recurrent rectal prolapse, we would repair the prolapse first, and do those procedures first, and then stage it, and later place the device.

MS. NEWMAN: And what would you recommend? Should they be evaluated first?

DR. CONGILOSI: That is part of our routine evaluation preoperatively. Most of them I do defacography on, or with evaluating them with a pelvic examine, and looking at those factors.

But if they have obvious pelvic prolapses, or a vaginal prolapse, I have to repair that first, because I think that would technically make it difficult to put the cuff in. And technically to go later and repair that.

And to go back in obviously to the lower abdomen, where the reservoir balloon is, one has to be careful of that incision in the tubing. So if we felt

that they needed surgery, if would be transabdominal. We would recommend that that be done first.

DR. SMITH: If you have erosion do you have to do a colocolostomy?

DR. CONGILOSI: If we have a revision?

DR. SMITH: If you have an erosion.

DR. CONGILOSI: An erosion?

DR. SMITH: Yes.

DR. CONGILOSI: No, we would usually just take the device out and then it would heal.

DR. SMITH: And then it would heal?

DR. CONGILOSI: Yes.

DR. KOLTUN: Doug presented 34 explants out of the original 115. Have any of those full explants been recent implants?

DR. CONGILOSI: Yes. Do we have the number on that, of the full explants that were reimplanted? Yes. The protocol was to wait 3 to 6 months if it was explanted for infection, and steering towards the 6 months range, and then to go back for a full reimplantation. So there are a number of those, yes.

DR. KOLTUN: Could you speak up? I'm sorry, but diabetics, that was a .00001. How many diabetics did you have and how many infections were there in that diabetic group?

CHAIRMAN KALLOO: I think there is a question about co-morbid data.

DR. CONGILOSI: We are still looking for the numbers on that, and --

CHAIRMAN KALLOO: Do you have that data available now, the co-morbid data, patients with co-morbidities?

MR. ANTIL: We are going to have to pull that up.

DR. KOLTUN: Okay. Then related to that is --

DR. CONGILOSI: Well, that explains it. It got reimplanted.

DR. KOLTUN: -- that with you being the most experienced, is there someone that you would say that I will not put this in you? Is there a patient that you would say I will not put this in you based upon my experience?

DR. CONGILOSI: Certainly.

DR. KOLTUN: And who is that someone?

DR. CONGILOSI: It takes morbidity to open and close the pump. If they don't have mobility, I would not do it. They need to be aware that -- I advise patients that there is about a 50 percent chance that they are going to need a revision, and if they are not mentally or psychologically up to that, I wouldn't do it.

If they have been -- there are some in the series that have been radiated, and I personally have not placed anyone who has had radiation in their perineum. Those would be the big categories of patients that I would not do it in.

DR. KOLTUN: Would you do it in a transplant patient on immunosuppressants?

DR. CONGILOSI: No. Well, I would qualify that; unless their transplant -- well, we have had somebody who has come for a consult regarding that who is 12 years out from that transplant, and are on minimal immunosuppressants and it is in discussion right now, because we are not sure on that patient.

The opinion of the transplant surgeon is that they could have it done, and they have also had an other implant done for another reason successfully.

DR. TALAMINI: And as a follow-up to that question, and this may not be a fair question. So if it is, don't answer. Based upon what you have said, and if you are familiar with the proposed labeling for this device, are you happy with it as it exists, the proposed labeling for the device? That is, if you are familiar enough with it.

DR. CONGILOSI: I don't think I am familiar enough with how the labeling is right now.

CHAIRMAN KALLOO: Karen.

DR. WOODS: I have a couple of very specific questions about some of the numbers. The first one is that in the data it says you had failure FISS at 12 months according to the point score in 10 patients, with 59 successes.

What was the reason if you know for the failure in those 10 patients? These were not listed as explants. It just says failure. Why did they fail?

DR. CONGILOSI: Let me pull those up.

MR. WORRELL: David Worrell, American Medical Systems. If they were listed as failure in the FISS analysis, they did not achieve the 24 point drop.

DR. WOODS: Right, I understand that, but what do you think the reason for that is? Is there something specific about those patients that led to failure? Was it a device that was too big, too small, or what was the reason for that?

DR. CONGILOSI: The ones that I can speak of are antidotally the ones in my series, and which are similar to some of the other groups. It may have been that the cuff was too large due to tissue atrophy, and they hadn't yet undergone a revision, and subsequently underwent a revision.

And that is true of at least one patient who subsequently got diagnosed with cancer and for that reason, for an unrelated cancer, was not going to undergo revision.

The other possibility would be poor patient selection in at least one patient who

continued to abuse laxatives even afterwards, and would just sort of binge and purge, and still be incontinent.

So some of the etiologies were those medically related things, and one category certainly is for patients who may have needed a cuff change and had not yet undergone that surgery.

DR. WOODS: And surely there must be a list of who those 10 patients are and what their problems were?

MR. WORRELL: Yes, we have that data, and we can put that together during the meeting and provide that to you towards the end of the meeting.

DR. WOODS: Okay. Secondly, of the 34 explants, it says 27 exited entirely, and seven were appropriate for reimplant. Can you say why the other 27 were not appropriate for reimplant? Was that patient choice, or was there something anatomically? Was it an erosion or what was the breakdown of those who were not appropriate for reimplant and why?

DR. CONGILOSI: Patient choice not to undergo reimplantation, and the decision by the

patient to then go to a stoma. That was the common reason for that. And in one patient a decision that they were medically not fit due to subsequent cardiac events.

DR. WOODS: So did most of those patients ultimately have a stoma placed?

DR. CONGILOSI: Well, 9 out of the 27 had a stoma placed.

DR. WOODS: And the others are back to baseline, or we don't know if they are even worse?

DR. CONGILOSI: Correct.

DR. MCCLANE: Do you know the FISS scores of those 27?

DR. CONGILOSI: We don't have that sub-analysis.

DR. MCCLANE: Because they probably were not followed up on?

DR. CONGILOSI: Right. If they are explanted, then further scoring is not done. So we would not have a score after explant.

DR. EPSTEIN: In the patients in whom the Neosphincter did not work, and in whom the sphincter

was ineffective, did you look at the anorectal manometry pre-and-post? Do you have any information on that and as to why the device didn't work?

DR. CONGILOSI: Well, I think you will see some studies in the literature, but manometry has not been predictive of success with the cuff, which is not surprising. Manometry is not predictive of success with other operations.

DR. EPSTEIN: I understand. I was wondering if there was any data there at all that looked at that. I mean, you looked at it pre-procedure, and I was wondering if you looked at it post-procedure at all.

DR. CONGILOSI: We did follow manometry looking at how it related to the degree of continence.

DR. EPSTEIN: I guess my broader question is why didn't the sphincter work in some cases? What was the major reason why it wasn't working?

DR. CONGILOSI: I don't specifically recall those patients, because it would be a variety.

CHAIRMAN KALLOO: It sounds as if you have some data pulling to do for us. Could we just move